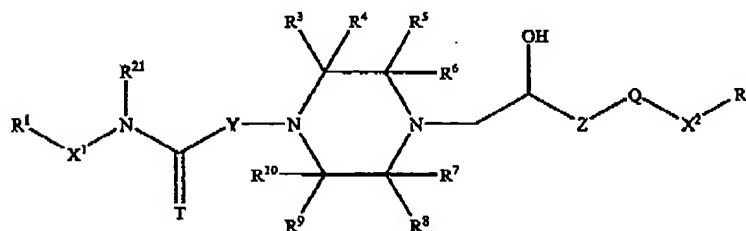


Response to October 12, 2005, Office Action  
 Atty Dkt No. 02-0175  
 Application No. 10/729,499

# APPENDIX B

## CLEAN COPY OF CLAIMS AS AMENDED HEREIN

1. A compound of the formula:



wherein:

R<sup>1</sup> is aryl or heteroaryl optionally substituted with 1 to 3 substituents selected from acetyl, alkyl, hydroxy, alkoxy, halogen, halogen substituted alkyl, phenyl, and phenyl substituted with acetyl, alkyl, alkoxy, hydroxy, halogen, or halogen substituted alkyl;

R<sup>2</sup> is heteroaryl optionally substituted with 1 to 3 substituents selected from acetyl, alkyl, hydroxy, alkoxy, halogen, halogen substituted alkyl, phenyl, and phenyl substituted with acetyl, alkyl, alkoxy, hydroxy, halogen, or halogen substituted alkyl

X<sup>1</sup> is a covalent bond, or -(CR<sup>15</sup>R<sup>16</sup>)<sub>p</sub>-, in which R<sup>15</sup> and R<sup>16</sup> are independently hydrogen, hydroxy, lower alkyl, or -C(O)OR<sup>17</sup>, in which R<sup>17</sup> is hydrogen, lower alkyl, or optionally substituted phenyl, and p is 1, 2 or 3; with the proviso that when p is 1, R<sup>15</sup> and R<sup>16</sup> cannot be hydroxy;

R<sup>21</sup> is hydrogen or lower alkyl;

T is oxygen or sulfur;

Y and Z are -(CR<sup>18</sup>R<sup>19</sup>)<sub>q</sub>- and q at each occurrence is 1, 2 or 3, in which R<sup>18</sup> and R<sup>19</sup> at each occurrence is hydrogen or lower alkyl; and

Response to October 12, 2005, Office Action  
Atty Dkt No. 02-0175  
Application No. 10/729,499

$R^3, R^4, R^5, R^6, R^7, R^8, R^9$ , and  $R^{10}$  at each occurrence are hydrogen, lower alkyl, or -  
 $C(O)R$ ; in which  $R$  is  $-OR^{11}$  or  $-NR^{11}R^{12}$ , where  $R^{11}$  and  $R^{12}$  are hydrogen or lower  
alkyl; or  
 $R^3$  and  $R^4, R^5$  and  $R^6, R^7$  and  $R^8, R^9$  and  $R^{10}$ , when taken together with the carbon to  
which they are attached, represent carbonyl;  
 $Q$  is oxygen, sulfur, or  $-NR^{20}$ , in which  $R^{20}$  is hydrogen or optionally substituted lower  
alkyl;  
 $X^2$  is a covalent bond or  $-(CR^{18}R^{19})_q$ - wherein  $q$  at each occurrence is 1, 2 or 3, and  $R^{18}$   
and  $R^{19}$  at each occurrence is hydrogen or lower alkyl; and  
with the proviso that when  $X^1$  is a covalent bond and  $Y$  is  $-(CR^{18}R^{19})_q$ - in which  $q$  is 1 and  
 $R^{18}$  and  $R^{19}$  are hydrogen, then  $R^1$  is not optionally substituted phenyl.

3. The compound of claim 1, wherein  $R^3, R^4, R^6, R^7, R^8, R^9$ , and  $R^{10}$  at each  
occurrence are hydrogen and  $R^5$  is hydrogen or methyl.

4. The compound of claim 3, wherein  $Q$  and  $T$  are both oxygen and  $X^2$  is a  
covalent bond.

5. The compound of claim 4, wherein  $R^{21}$  is hydrogen,  $Y$  is methylene or  
ethylene, and  $Z$  is methylene.

6. The compound of claim 5, wherein  $R^1$  is optionally substituted aryl.

7. (The compound of claim 6, wherein  $R^2$  is optionally substituted  
benzothiazolyl or optionally substituted benzoxazolyl.

8. The compound of claim 7, wherein  $R^1$  is indan-4-yl,  $R^2$  is 2-  
methylbenzothiazol-5-yl,  $R^5$  is hydrogen, and  $X^1$  is a covalent bond, namely 2-{4-[(2R)-2-  
hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-indan-4-ylacetamide.

Response to October 12, 2005, Office Action  
Atty Dkt No. 02-0175  
Application No. 10/729,499

9. The compound of claim 7, wherein R<sup>1</sup> is (1,2,3,4-tetrahydronaphth-1-yl, R<sup>2</sup> is 2-methylbenzothiazol-5-yl, R<sup>5</sup> is hydrogen, and X<sup>1</sup> is a covalent bond, namely 2-{4-[(2R)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-((1S)(1,2,3,4-tetrahydronaphthyl))acetamide.

10. The compound of claim 7, wherein R<sup>1</sup> is naphth-2-yl, R<sup>2</sup> is 2-methylbenzothiazol-5-yl, R<sup>5</sup> is hydrogen, and X<sup>1</sup> is -CH(CH<sub>3</sub>)-, namely 2-{4-[(2R)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-((1S)-1-(2-naphthyl)ethyl)acetamide.

11. The compound of claim 7, wherein R<sup>1</sup> is phenyl, R<sup>2</sup> is 2-methylbenzothiazol-5-yl, R<sup>5</sup> is hydrogen, and X<sup>1</sup> is -CH(CH<sub>3</sub>)-, namely 2-{4-[(2R)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-((1S)-1-phenylethyl)acetamide.

12. The compound of claim 6, wherein R<sup>1</sup> is optionally substituted heteroaryl and R<sup>2</sup> is optionally substituted benzothiazolyl or optionally substituted benzoxazolyl.

13. The compound of claim 12, wherein R<sup>1</sup> is 4-(4-chlorophenyl)thiazol-2-yl, R<sup>2</sup> is 2-methylbenzothiazol-5-yl, R<sup>5</sup> is hydrogen, and X<sup>1</sup> is a covalent bond, namely 2-{4-[(2R)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-[4-(4-chlorophenyl)(1,3-thiazol-2-yl)]acetamide.

14. The compound of claim 12, wherein R<sup>1</sup> is 4-(4-chlorophenyl)thiazol-2-yl, R<sup>2</sup> is 2-methylbenzothiazol-5-yl, R<sup>5</sup> is methyl, and X<sup>1</sup> is a covalent bond, namely 2-{4-[(2R)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]-3-methylpiperazinyl}-N-[4-(4-chlorophenyl)(1,3-thiazol-2-yl)]acetamide.

15. The compound of claim 12, wherein R<sup>1</sup> is 9-ethylcarbazol-3-yl, R<sup>2</sup> is 2-methylbenzothiazol-5-yl, R<sup>5</sup> is hydrogen, and X<sup>1</sup> is a covalent bond, namely 2-{4-[(2R)-2-

Response to October 12, 2005, Office Action  
Atty Dkt No. 02-0175  
Application No. 10/729,499

hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-(9-ethylcarbazol-3-yl)acetamide.

16. The compound of claim 12, wherein R<sup>1</sup> is 6-quinolyl, R<sup>2</sup> is 2-phenylbenzoxazol-5-yl, R<sup>5</sup> is hydrogen, and X<sup>1</sup> is a covalent bond, namely 2-{4-[(2R)-2-hydroxy-3-(2-phenylbenzoxazol-5-yloxy)propyl]piperazinyl}-N-(6-quinolyl)acetamide.

17. The compound of claim 12, wherein R<sup>1</sup> is 8-quinolyl, R<sup>2</sup> is 2-methylbenzothiazol-5-yl, R<sup>5</sup> is hydrogen, and X<sup>1</sup> is a covalent bond, namely 2-{4-[(2R)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-(8-quinolyl)acetamide.

18. A method of treating a disease state chosen from diabetes, damage to skeletal muscles resulting from trauma or shock and a cardiovascular disease selected from the group consisting of atrial arrhythmia, intermittent claudication, ventricular arrhythmia, Prinzmetal's (variant) angina, stable angina, unstable angina, congestive heart disease, and myocardial infarction in a mammal by administration of a therapeutically effective dose of a compound of claim 1.

19. The method of claim 18, wherein the disease state is a cardiovascular disease selected from atrial arrhythmia, intermittent claudication, ventricular arrhythmia, Prinzmetal's (variant) angina, stable angina, unstable angina, congestive heart disease, and myocardial infarction.

20. The method of claim 18, wherein the disease state is diabetes.

21. A pharmaceutical composition comprising at least one pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of claim 1.